Leukemia Research 35 (2011) e175–e176

Contents lists available at ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Letter to the Editor

Haematological and cytogenetic responses after only 7 days of Lenalidomide in a patient with myelodysplastic syndrome and chromosome 5q deletion

1. Introduction

Lenalidomide (LEN) is an immunomodulatory drug (IMID) with dramatic efficacy on the anemia of International Prognostic Scoring System (IPSS) low and intermediate 1 (lower risk) myelodysplastic syndrome (MDS) with 5q deletion, leading to red blood cell (RBC) transfusion independence and complete cytogenetic response in 67% and in 45% of the patients, respectively [1]. Responses to LEN are generally seen after 4 to 16 weeks of treatment. In responders, although the optimal duration of LEN is unknown, the recommendation is to continue treatment until relapse [2]. We report a patient with lower risk MDS with 5q deletion who achieved RBC transfusion independence after only 7 days of LEN, during 8 months

2. Case report

A male patient, born in 1947, was referred in August 2006 for anemia. A complete blood count (CBC) showed severe anemia with Hb = 6.9 g/dl, normal MCV, low reticulocytes, WBC of 1.8 G/l with ANC of 0.72 G/l with a normal platelet count of 190 G/l. A bone marrow aspirate showed cellular bone marrow, with abundant dysplastic megakaryocytes with small monolobated nuclei, 51% erythroblasts, with signs of dysplasia, hypogranulated and hyposegmented granulocytes, and marrow blasts <5%. The bone marrow karyotype showed del (5)(q14, q34) in 8 of 15 mitoses examined. A diagnosis of MDS with isolated 5q deletion and intermediate 1 IPSS was made. The patient was started on a program of RBC transfusions until February 2007, at a rate of 2 units packed RBC/month with iron chelating therapy with deferoxamine, initiated in January 2007. Treatment with thalidomide was started in February 2007 at a dose of 50–100 mg/d, depending on side effects, and resulted in transfusion independence and an increase in Hb level to 11 g/dl during 22 months, but relapse occurred in December 2008, and a transfusion program (2 units packed RBC/2 weeks) restarted along with iron chelating treatment with Deferasirox. In June 2010, thrombocytopenia (platelet count of 80 G/l) developed, while ANC was 0,8 G/l and the bone marrow smear was unchanged with 2% blasts. The karyotype showed, in addition to del (5)(q14, q34) in 8 mitoses, appearance of an other clone with isolated trisomy 8 (2 mitoses) while 10 mitoses were normal. Lenalidomide was prescribed at a dose of 15 mg/d (the only available dosage of Lenalidomide in Tunisia) during 1 week (from 9 to 15 June 2010), and subsequently discontinued as the drug became unavailable. No cytopenias were noted. The patient achieved transfusion independence after 3 weeks (last RBC transfusion performed on 7 July 2011) and the Hb level rose to 11.4 g/dL, a response which was sustained during 8 months, until March 2011 when anemia recurred, and RBC transfusion was necessary. The bone marrow karyotype performed 5 months after Lenalidomide treatment showed del 5q in 14 of 20 mitoses examined but with disappearance of trisomy 8.

3. Comments

In spite of the very short treatment duration (7 days, due to the difficulty in obtaining Lenalidomide in Tunisia), the patient achieved erythroid response and RBC transfusion independence, of 8 months duration. This is the shortest LEN treatment duration reported with response in lower risk MDS with del 5q, to our knowledge. So far, the minimal reported LEN treatment duration associated with a response was 28 days [3]. This hematological response was accompanied with the disappearance of the additional trisomy 8, but not of del 5q. One of the main mechanisms of action of Lenalidomide in lower risk MDS with del 5q appears to be direct suppression of the MDS clone, especially through inhibition in del 5q cells of the haplo insufficient cell cycle regulatory proteins cdc25c and PP2A alpha, promoting their selective G2 arrest and apoptosis [4]. The present case report would therefore suggest that, in some patients, LEN administration during 7 days is sufficient to obtain significant reduction of the del 5q clone, compatible with a relatively durable erythroid response but not with achievement of cytogenetic remission. Alternatively, other potential mechanisms of action of LEN in MDS, including immunomodulatory and antiangiogenic effects, or direct stimulation of erythropoiesis [5] may have explained the current response. Interestingly, our patient had previously obtained an erythroid response with thalidomide, another IMID which, in MDS, appears to give similar erythroid response rates in patients with or without del 5q [6] and whose mechanism of action in MDS does not appear to include selective inhibition of del 5q clones

Funding source

None.

Conflict of interest statement

All authors have no conflict of interest to declare.

Acknowledgements

We would like to thank Naourez Ajmi, Moez Medhaffar, Hatem Bellaaj from the Department of Hematology, University of Sfax, HediChaker Hospital, Sfa, Tunisia.

References

[1] List A, Dewald G, Bennett J, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. N Eng J Med 2006;355:1456–65.

0145-2126/$ – see front matter
doi:10.1016/j.leukres.2011.05.020

[2] Giagounidis A, Fenaux P, Mufti GJ, et al. Practical recommendations on the use of Lenalidomide in the management of myelodysplastic syndromes. Ann Hematol 2008;87:345–52.
[3] Giagounidis A, Haase S, Heinsch M, Schlegelberger B, Aul C. Lenalidomide in the context of complex karyotype or interrupted treatment: case reviews of del(5q)MDS patients with unexpected responses. Ann Hematol 2007;86:133–7.
[4] Wei S, Chen X, Rocha K, et al. A critical role for phosphatase haplodeficiency in the selective suppression of deletion 5q MDS by Lenalidomide. Proc Natl Acad Sci USA 2009:10612974–9.
[5] Heise C, Carter T, Schafer P, Chopra R. Pleiotropic mechanisms of action of Lenalidomide efficacy in del(5q) myelodysplastic syndromes. Expert Rev Anticancer Ther 2010 Oct;10(10):1663–72.
[6] Kelaidi C, Park S, Brechignac S, et al. Treatment of myelodysplastic syndromes with 5q deletion before the lenalidomide era; the GFM experience with EPO and thalidomide. Leuk Res 2008;32:1049–53.

Sondes Hadiji Mseddi*
Faten Kallel
Olfa Kassar
Moez Elloumi
Department of Hematology, University of Sfax, HediChaker Hospital, Sfax, Tunisia

Ines Jedidi
Hematology Laboratory, Habib Bourguiba Hospital, Sfax, Tunisia

Halima Sennana
Cytogenetic laboratory, University of Sousse, FarhatHached Hospital, Sousse, Tunisia

Pierre Fenaux
Department of Hematology, Avicenne Hospital, Paris 13 University, Paris, France

* Corresponding author at: Department of Hematology, University of Sfax, HediChaker Hospital, Route Al Ain, 3029, Sfax, Tunisia. Tel.: +216 74 240 549; fax: +216 74 240 549.
E-mail address: sondes.mseddi@rns.tn (S. Hadiji Mseddi)

26 April 2011

30 April 2011

16 May 2011
Available online 11 June 2011